## **Sharing Solutions** for Childhood **Obesity**

According to a 2004 report by the Institute of Medicine Committee on Prevention of Obesity in Children and Youth, approximately 9 million American children over 6 years of age are considered obese—that is, they have a body mass index (BMI) equal to or greater than the 95th percentile as calculated by the Centers for Disease Control and Prevention (CDC). Yet most experts believe the 9 million figure is minimal. Rates of obesity also are much higher among some popurelated to environment and obesity. This year, the focus was on solutions.

"The goal of the conference was to try to identify the successful environmental interventions that have been developed across the country, and then to disseminate them more broadly," said primary organizer Allen Dearry, NIEHS associate director for research coordination, planning, and translation. "The major accomplishment was to bring together a very interdisciplinary group of experts in environmental health sciences, and in fields like planning and transportation, and policy makers to work together and think collaboratively, and to be able to define what makes one of these successful environmental interventions work."

## **NIEHS Environmental Solutions to Obesity** in America's Youth Nutrition Behavior Families Schools Prevention Disparities The Washington Convention Center Washington, DC Communities http://www.niehs.nih.gov/drcpt/events/oe2005 National Institutes of Health U.S. Department of Health & Human Services

lations and in certain geographic areas. And the prevalence of childhood obesity is growing exponentially. In the past three decades, it has more than doubled in children aged 2-5 and 12-19, and more than tripled in children aged 6-11.

There is currently a wide variety of activity at all levels aimed at reducing the epidemic of childhood obesity, as shown by the gathering of more than 700 experts from many fields in early June 2005 for Environmental Solutions to Obesity in America's Youth, a conference sponsored by the NIEHS. The meeting followed up on the success of a similar event held in 2004, which was aimed primarily at identifying research opportunities and needs to help design a research agenda

The conference was supported in part by the Robert Wood Johnson Foundation. The planning committee included representatives from the NIH, the CDC, and the U.S. Department of Transportation, as well as from state and local health departments, academia, and the American Planning Association. Keynote speakers included NIEHS director David Schwartz, U.S. surgeon general Richard Carmona, CDC director Julie Gerberding, former National Football League star Lynn Swann (who is now the chairman of the President's Council on Physical Fitness and Sports), U.S. Department of Health and Human Services secretary Michael Leavitt, and Arkansas governor Mike Huckabee.

### Pinpointing the Factors

As several participants pointed out, human genetics and biology don't change quickly enough to account for spiking obesity rates of the past 30 years, so a complex array of environmental factors that influence individual behavior is clearly at the root of the epidemic, in both children and adults. At a press conference announcing the forthcoming awarding of \$5 million in NIH/CDC research grants addressing obesity and the environment, Schwartz said that defining the interface between environmental components and individual choices will be crucial to building a solid evidence base to support and refine efforts to stem the obesity tide.

"There's a fine balance between the environment and the individual that allows some people to make the choice for a more active and healthier life, and others to continue to eat the wrong types of foods or not be involved in physical fitness programs," Schwartz said. "That balance is very difficult to understand, and that's the focus of this research program and this conference."

The stakes involved are high. Obesity greatly increases a child's risk in adulthood of developing and dying from serious chronic conditions such as cardiovascular disease, type 2 diabetes mellitus, and certain cancers. Further, many children already suffer from adverse health effects related to their obesity.

Hypertension, until recently virtually unseen in young people, now strikes an estimated 4.5% of obese school-age children. Type 2 diabetes, also once considered rare in youngsters, is

now showing up more frequently (the CDC is currently investigating incidence and prevalence). In addition, obese youth often suffer from impaired quality of life, emotional effects such as poor self-image, elevated cholesterol, orthopedic conditions, liver diseases, sleep apnea, and metabolic syndrome (a cluster of disorders that increases risk of heart disease and diabetes), among other negative outcomes. If left unchecked, the public health burden of childhood obesity will only continue to increase.

### Finding Common Ground

Speaker David McCarron described the work of Shaping America's Youth (SAY), a public–private partnership that recently conducted a national survey of programs directed at physical activity and nutrition in children. SAY has established a national registry of such initiatives and is now approaching 2,500 program entries, with overall expenditures estimated at \$3.9–7.1 billion. SAY's mission is to define the scope of those efforts and to make its information widely accessible. The goal is to foster dialogue at the community level, and ultimately develop a national action plan to combat childhood obesity.

"People are committed, but the problem is [the effort to address childhood obesity is] not organized, it's not being sustained, it's probably not directed at the right age group, and we need to take this commitment and interest and really get it focused . . . on the very youngest children and their families," said McCarron, who is executive director of SAY. "We have to get to common goals, common language, common standards." He added, "They'll be modified community by community, and for each family they may be different, but we have to get to some very fundamental messages."

SAY will be conducting a series of town hall meetings over the next year in Memphis, Dallas, Philadelphia, and several California cities to get feedback from demographically representative community members. "It's not so much about teaching them something," McCarron explained. "We need to hear at a local level from the communities and the families as to what they see the problem as, what the barriers are. Otherwise, whatever we come away with from these national meetings might be totally disconnected."

The local socioeconomic environment, with often profound disparities in physical and financial access to healthy foods and physical activity, may contribute to the obesity epidemic, particularly among minority groups, who tend to suffer even higher obesity rates than the general population. Adam Drewnowski, director of the Center for Public Health Nutrition at the University of Washington, addressed this concept and showed that in his area of Washington state, geographic information system mapping of the distribution of obesity rates demonstrated an association of higher obesity rates with lower socioeconomic status and limited access to healthy foods. Using that type of methodology to tease out associations at the local level will be critical to successfully combating the problem, Drewnowski said.

### **Growing Smarter**

The effect of sprawling development on sprawling waistlines was a subject of particular scrutiny at the conference. Roland Sturm, a senior economist at RAND, presented data from his recent unpublished national study of the impact of suburban sprawl on the development of chronic health conditions, including obesity. He found that greater sprawl was associated with an increase in chronic health problems, with the strongest associations with heart disease, abdominal and digestive problems, migraines and headaches, arthritis and joint pain, and trouble breathing. The study also suggested a relation between sprawl, reduced walking, and higher BMI.

"Smart growth" may be one approach that can help reverse these trends. Former Maryland governor Parris N. Glendening, who is now president of the nonprofit Smart Growth Leadership Institute, believes that incorporating opportunities for physical activity into built environment design is an important part of the mix to fight childhood obesity. "If we continue to build environments that discourage physical activity, we're going to continue to contribute to the problem," he said.

The Smart Growth Leadership Institute urges policy makers to take a broader, more long-term view of the potential impact of their decisions regarding the built environment and health. Policy changes encouraging mixed-use zoning and actual mixed land use—such as the shift of funds to public transit, the creation of sidewalks and bicycle paths, and the preservation of open spaces—are critical to the smart growth concept.

"If we can make the health and physical activity variables a part of the planning and land use discussion, we can have a significant impact," Glendening said. "It's not going to occur overnight, but we can see all across the country whole communities . . . where this mixed-land-use urban walkability is taking place, creating a fun community where you want to be out and about."

### A Variety of Venues

The battle against childhood obesity is being fought on many different fronts. The conference highlighted several nongovernmental initiatives that are addressing the problem in imaginative ways, with the goal of sharing what's working and what isn't.

Kaiser Permanente has adopted a strategy of emphasizing prevention of child-hood obesity in its programs. Among other efforts, the company has trained

more than 1,000 pediatricians and family physicians on ways to promote physical activity and dietary behavior change in patients and their families. The organization is also actively engaged in anti-obesity coalitions and partnerships through its Healthy Eating, Active Living (HEAL) program.

Girls on the Run, a 12-week program aimed at third- to fifth-grade girls, combines training for a five-kilometer run with life skills development and lessons to enhance self-esteem, all of which can help reduce or prevent obesity. Founded by Molly Barker in 1996, the program is now active in 120 U.S. and Canadian cities, with more than 50,000 girls participating.

The media environment is an influential element in the obesity landscape, in both negative and positive ways. New opportunities to entice young people toward unhealthy food choices are proliferating. Patti Miller, vice president of Children Now, a national child advocacy organization based in California, told attendees that the latest such threat is from interactive marketing. This often comes in the form of "advergames," online games promoted during TV shows that advertise unhealthy foods as part of the game. Children Now is lobbying the Federal Communications Commission to ban such practices in children's television programming.

Meanwhile, Sesame Street, with its large audience of preschool children, has launched a multiyear, content-driven initiative called Healthy Habits for Life. The program, which will be incorporated into all of Sesame Street's media outlets (television, video, books, magazines, and online), promotes healthy habits as being just as critical to early development as learning to read and write.

Food and beverage giant PepsiCo has recognized that there is a tremendous business opportunity in offering consumers more nutritious, healthful products, according to vice president of marketing for health and wellness Ellen Taaffe. Health-oriented products are now the company's fastest-growing sector and currently represent almost 40% of the company's portfolio. Taaffe described several initiatives PepsiCo has undertaken to promote health and fitness, including the Smart Spot program, in which a symbol on a product's packaging identifies it as a healthy choice.

Cathleen Toomey, vice president of communications at Stoneyfield Farm, the nation's largest producer of organic yogurt, described that company's successful efforts to launch the first organic and healthy vending machines for schools. Produced in collaboration with the schools themselves, which receive the profits from sales, there are currently 32 machines in place at schools in seven states, with a waiting list of 930 schools.

Governmental efforts also received attention. These included state-level efforts in California and North Carolina as well as larger-scale programs such as Active Living by Design, a Robert Wood Johnson Foundation effort in 25 cities to increase physical activity through changes in community design, and America on the Move, a program working at the local, state, and national levels to encourage people of all ages to make small increases in walking and small decreases in caloric intake to prevent weight gain and improve health. In still another initiative, the Safe Routes to School program, several federal agencies including the U.S. Department of Transportation are working to make walking and biking to school safe and appealing to children.

Another session highlighted several new tools, measures, and methods that have been developed to help reliably assess environment-obesity connections, such as assessments of park characteristics, urban design walkability, and aspects of the "nutrition environments" (the quality and availability of foods, and types of food outlets in discrete settings such as schools and neighborhoods). These methodological advances will help to provide a muchneeded validated evidence base for use in evaluating the effectiveness of obesity treatment and prevention programs. Many participants commented that more longitudinal research is needed to see what does and doesn't work for preventing obesity.

The conference also marked the launch of a major new trans-NIH initiative called We Can! (Ways to Enhance Children's Activity & Nutrition). Spearheaded by the National Heart, Lung, and Blood Institute, We Can! is a national public education outreach effort that will provide activities and programs that encourage good nutritional choices, more physical activity, and less television and computer screen time in 8- to 13-year-olds.

"What we're trying to do," said Carmona, "is have the American public appreciate that within their control, simple steps such as more physical activity and eating a healthy diet will reduce risk in their lives and improve their health status." There was a broad consensus at the conference that those simple steps are the best ways to both treat and prevent childhood obesity.

### Whittling Away at Obesity

Although reversing the epidemic of childhood obesity will require long-term efforts and long-term commitments from all stakeholders, Dearry is optimistic that if certain aspects of the environment can be successfully modified, the explosive growth of childhood obesity can be at least reduced, if not eliminated, within the next 5-10 years. "I think these changes in the environment are not impossible," he says. "They can start with small steps rather than needing to be large-scale changes. Changes in the environment that enable people to have access to a better diet or more physical activity can start to lead to reversals in the trends we've seen."

Added Toomey: "The message I would encourage everyone to take away from this conference is that you can make small changes. You can start a Girls on the Run program, you can apply for a healthy vending machine. You can make the doors open, and we can whittle down childhood obesity piece by piece." **–Ernie Hood** 

## Growth Spurt for EDC Recognition

Once in a great while, a scientific conference takes place that later proves to have been a turning point in a particular field—a seminal event remembered long after the name tags have been discarded and the posters recycled. Although it's too soon to be certain, participants say the Forum on Endocrine Disrupting Chemicals, held 3 June 2005 in San Diego, may well come to be seen as a landmark in both the growth of the discipline and the progress of the science itself.

With the stated intent of bringing the science of endocrine-disrupting chemicals (EDCs) to the forefront, The Endocrine Society convened the workshop the day before its 87th annual meeting. Although EDCs have been on the society's agenda before, the forum was its first day-long, formally organized event devoted to the subject.

"We've had very scattered presentations of results from the NIEHS and the Environmental Protection Agency at the endocrine meeting from time to time, but it was really hard in the past to produce a great deal of interest," says Kenneth Korach, program director of the NIEHS Environmental Diseases and Medicine Program, who delivered the keynote address at the forum. "Now The Endocrine Society is taking a much more active role in expanding its interactions and development regarding the endocrine disruptor field, and there seems to be a strong commitment for supporting endocrine disruptor research and establishing a formal society program in EDCs."

Attendance at the forum—organized by prominent EDC researchers Andrea Gore, R. Thomas Zoeller, and Jerrold Heindel-included more than 200 toxicologists, epidemiologists, clinicians, and other members of the endocrinology community, indicating that the effort to reach across disciplines and encourage translation has been successful. Korach believes that increasing awareness of EDCs among clinicians is particularly important. "Some of the effects of EDCs that will be seen in humans will be picked up by . . . endocrinologists in their diagnosis of disorders as these patients present to them, so educating them will be very worthwhile in terms of translational research."

Korach and fellow NIEHS scientists Retha Newbold and John McLachlan (now at Tulane University) were among the pioneers in EDC research; today, Korach is encouraged by the field's progress. "Twenty-five or thirty years ago, it was a very small group, but now we're drawing more and more people into it from other disciplines," he said, "and that's a real success in terms of the education taking place at this forum."

#### In Utero and Beyond

Korach, Newbold, and several other speakers familiarized attendees with the latest and most significant concepts in the field, focusing to a large extent on the growing belief that exposure to EDCs in utero can result in gene-environment interactions that will cause susceptibility to disease or reproductive problems later in life. The developing embryo is thought to be particularly sensitive to exposure to even low doses of exogenous EDCs during critical periods in early development, especially during sexual differentiation and organ development. The synthetic estrogen diethylstilbestrol, a well-known human carcinogen, is perhaps the most famous example of an EDC with a potentially devastating impact following fetal exposure. This compound was prescribed

The forum also featured presentations reporting a variety of highly significant recent findings regarding the effects of EDCs. Work published 3 June 2005 in Science and presented by Michael Skinner, director of the Center for Reproductive Biology at Washington State University, could prove to have extraordinarily farreaching implications.

Skinner's group was researching the effects of two model EDCs-the antiandrogenic fungicide vinclozolin and the estrogenic pesticide methoxychlor—on embryonic testis development in mice. They discovered that exposing gestating mothers to the EDCs caused reduced sperm generation in adult male offspring. More importantly, as they continued to breed the animals, they found that the altered phenotype was retained all the way to the fourth generation—the male germ line had been permanently reprogrammed. "The human analogy is that your grandmother may have been exposed to an environmental toxicant, and two generations later, you might have a disease, even though you've never seen the toxicant—and then you could potentially pass it on to your grandchildren," says

The transgenerational effect was found to be epigenetic, caused by a chemical modification of DNA through methylation, as opposed to a normal base DNA mutation. Ninety percent of the offspring in each generation inherited the phenotype, a very high transmission frequency compared to that seen with genetic mutational events, which is typically 1% or less.

"Now we need to consider this transgenerational effect in our future analyses, doing transgenerational studies to see if the effects of a toxicant can actually be transferred to the subsequent generations," says Skinner. It will also be important to identify the types of compounds, including other EDCs, that may tend to have this effect. Skinner says this is among several lines of investigation his team will pursue.

Beyond the effects on male fertility, the group also found that as both the male and female animals aged, they experienced other disease states such as premature aging, prostate disease, kidney disease, and

### Headliners

### **Cadmium-Induced Disease** NIEHS-Supported Research



### Discovery of Gene Responsible for Cadmium Transport in Mice

Dalton TP, He L, Wang B, Miller ML, Jin L, Stringer KF, Chang X, Baxter CS, Nebert DW. 2005. Identification of mouse SLC39A8 as the transporter responsible for cadmiuminduced toxicity in the testis. Proc Natl Acad Sci USA 102:3401-3406.

Cadmium is a toxic and carcinogenic nonessential metal released from mining, smelting, battery manufacturing, and coal burning. Among other routes, humans are exposed to cadmium by smoking cigarettes and eating contaminated seafood or plants grown in contaminated soil. Environmental levels of cadmium have risen along with advances in industrialization, and the role of cadmium in human disease is therefore of increasing concern. Now NIEHS grantee Daniel W. Nebert and colleagues have discovered a gene responsible for the transport of cadmium in mice, which hints at a target that could be employed to prevent the toxic effects of cadmium in humans.

Cadmium is readily absorbed through the lungs, intestines, and skin, and accumulates in the kidneys. The toxic mechanisms of cadmium are not well understood, but it is known to act intracellularly, causing damage particularly to the lungs, kidneys, bone, central nervous system, and reproductive tissues. Cadmium is also known to cause abnormalities in the developing embryo. The testis is a sensitive marker of cadmium exposure; cadmiuminduced testicular necrosis is common across all studied animal species having testes. Exposure to this metal is a significant problem in many developing countries, where undernourishment and iron deficiency are associated with increased cadmium toxicity.

Nebert and colleagues administered low doses of cadmium to mice and demonstrated that the SLC39A8 (ZIP8) protein, coded by the SIc39a8 gene, transported cadmium to the testis, causing vascular endothelial cell injury and subsequent testicular tissue death. Using in vitro models, the research team found that vascular endothelial cells from cadmium-insensitive mice did not accumulate ZIP8 mRNA, whereas cells from cadmium-sensitive mice did. The team suggests, therefore, that loss of vascular endothelial ZIP8 mRNA expression in the insensitive strains protected the mice's testes against cadmium toxicity.

Nebert and colleagues suspect that ZIP8 is normally responsible for the transport of other metals such as manganese and zinc, and that cadmium "participates as an opportunistic hitchhiker." Because humans carry the analogous SLC39A8 gene, these findings have identified a potential target for exploration in preventing the toxic effects of cadmium in exposed people. -Jerry Phelps



**Beginning a lifetime of vulnerability.** A recent meeting highlighted new data showing that *in utero* exposures to endocrine-disrupting chemicals can initiate changes leading to disease later in life.

tumor development. This implies that the epigenetic transgenerational effects of an environmental exposure may actually constitute a previously unrecognized disease mechanism. Identifying the genes with this reprogrammed methylation pattern that are transgenerational could lead to the development of many new diagnostic markers or therapeutic targets. Skinner and his colleagues are now in the early stages of establishing candidate genes and exploring their correlation with certain diseases.

Finally, the discovery raises the possibility that any environmental factor with an epigenetic effect could play a significantly more important role in evolutionary biology than previously suspected. "If you have a subpopulation of animals that are exposed and gain this permanent genetic phenotype, then you actually could potentially change the evolution of that species," Skinner explains. "This could explain and provide a mechanism for some unknown parameters in evolutionary biology."

#### Reproduction Ramifications

In another presentation, Shanna Swan, a professor of obstetrics and gynecology at the University of Rochester Medical Center, shared the results of her group's

investigation—the first of its kind in humans-of the effects of prenatal phthalate exposure on male testicular development. Phthalates are a common class of chemicals used in many household products, plastics, and cosmetics, and population studies have shown that virtually everyone carries some level of body burden of the compounds. In a study published in the August 2005 issue of EHP, the team found, consistent with previous rodent studies on phthalate exposure, an association between elevated intrauterine phthalate concentrations and adverse effects on male infants' genital characteristics that serve as markers for normal sexual development, particularly the distance between the anus and the base of the penis.

"The idea is that the development of the testes is interrupted in fetal life, and that this has consequences in adult life, as well as at birth," says Swan. "We've certainly seen that [effect] in rodents, and this is the first evidence that it may occur in humans as well." [For more information on this study, see "Phthalates and Baby Boys," p. A542 this issue.]

Two other presentations at the forum were particularly noteworthy. In one, Frederick vom Saal, a professor in the Division of Biological Sciences at the University of Missouri–Columbia, described several of his group's studies into the interactive effects between varying levels of bisphenol A and fetal endogenous estradiol.

Bisphenol A is used extensively as a liner in canned goods, and in polycarbonate plastic products such as baby bottles, water bottles, and laboratory equipment including animal cages and feeding and watering equipment. The chemical has been shown to leach in bioactive amounts from such products, particularly when they are scratched or worn. According to vom Saal, this could represent a previously unrecognized source of disruption to laboratory experiments, with bisphenol A exposure impacting hormonal activity in experimental animals.

Even at very low doses of bisphenol A—well below the "no effect" concentrations recognized in current regulations—vom Saal and colleagues have seen prostate deformities in experimental animals associated with minute changes in background fetal estradiol levels. He told attendees that, given the understanding that the fetus is extremely sensitive to very small changes in estrogen, it seems clear that the levels of bisphenol A that leach out of products constitute a threat to human health.

In the other presentation, graduate student Stefanie Whish of Northern Arizona University in Flagstaff described research to be presented at the main meeting suggesting that uranium in its soluble form is an EDC, and may contribute to reproductive health problems in the Navajo people. Whish and her colleagues treated ovariectomized mice with uranyl nitrate in drinking water. Despite the absence of ovaries, the animals exhibited estrogen-like responses to the uranyl nitrate exposure, suggesting that the compound is estrogenic and possibly an EDC. These results were observed at the EPA's safe drinking water concentration level for uranyl nitrate, which is exceeded in many drinking water sources in the Four Corners region of the Navajo nation.

With scientific evidence mounting that EDCs may have profound and complex effects upon human health, it is becoming increasingly clear that a comprehensive, multidisciplinary approach will be needed to gain the knowledge necessary to accurately assess risk and develop therapies. Only time will tell, but this forum may be seen as a landmark event in achieving the critical mass of cross-disciplinary interest, enthusiasm, and communication that will result in important new discoveries in the future. **–Ernie Hood** 

BEYOND THE BENCH

# **Teaching Teens by Setting the Scene**

For many teenagers, summer is a time for blockbuster movies, often featuring catastrophic natural—or alien-caused—disasters. For the last four years the Boston University Superfund Basic Research Program (BU SBRP) Outreach Core and the Boston Area Health Education Center (BAHEC; a program of the Boston Public Health Commission) have helped spice up local teens' summers by using this fascination with disaster scenarios to empower youth to think about their connection to the environment.

The Environmental Health Disaster Scenario program conducts group rolemodeling activities based around contamination or pollution emergencies at the beginning of the BAHEC's Youth to



Health Careers Summer Program as part of a health expo that features different careers in public health. Students learn how complicated public health decision making can be, and how quickly decisions must sometimes be made. The scenarios place the students in roles they might not normally find themselves in—as an environmental expert or public health official, for example. They also give the students a glimpse at potential public health careers beyond the familiar ones such as nursing, medicine, or pharmacy.

BAHEC, the local branch of a nationwide, federally funded program seeking to diversify, increase awareness of, and improve the quality of the health care service system, works with local universities, public school systems, and community agencies to recruit students for the summer program. The students are aged 14–18 and live in disadvantaged neighborhoods of Boston.

Each scenario exercise lasts about two hours and can involve as many as 100 or as few as 15 students. Madeleine Kangsen Scammell, outreach coordinator for the BU SBRP, says the scenarios are modeled after workshops that public health officials conduct to prepare for a public health emergency. In each scenario, several students take on the role of public health officials presented with an environmental health emergency and must work through possible questions and concerns that might arise. The students interview different people who could be affected by the scenario, from concerned residents to environmental experts to business owners (these roles are played by BU SBRP investigators and BU School of Public Health faculty members). After interviewing these community stakeholders, the students formulate and present their final decisions on how to address the problem.

Among other scenarios, students have had to decide how to deal with the discovery of dioxin-contaminated chickens on a poultry farm and whether to spray pesticides to control West Nile virus. Scenarios such as these teach the students how to identify possible risks associated with each environmental hazard, and provide insight into the media's role in influencing public opinion. In the case of the dioxin-contaminated chicken, participants examine the processing and distribution of the food to see where the contamination might have originated. They also discover what role government agencies play in protecting the public's health by regulating different phases of food production. In the West Nile virus scenario, students consider the possible dangers of spraying pesticides in neighborhoods—a current concern in Boston. They must also balance these dangers against the risks of infection with the virus.

The scenarios encourage the students to form, express, and support their own opinions, which they do with great enthusiasm. "The students get very excited when defending their decisions, and although we do not set the scenario up as a debate, it often turns into one," says Scammell. "Each team defends their decision as if it were the real thing. Sometimes they run for the mic when their turn has passed, wanting to respond to a point that has been made. No one sits still during the report-back."

The outreach partners are constantly adapting and improving the program model, and feel that it can be easily replicated by interested organizations. The materials are available for free online at http://www.bu.edu/bahec/. -Tanya Tillett